AN - PREV200300165352

RN - 78281-72-8 NEPAFENAC;7782-44-7 OXYGEN

TI - Topical Ocular Delivery of Nepafenac Inhibits Preretinal Neovascularization.

AB - Purpose: COX II activation has been implicated in ischemia-related VEGF upregulation and pathologic angiogenesis. Nepafenac, a topically delivered NSAID, has excellent corneal penetration. We investigated the utility of nepafenac against posterior segment neovascularization following topical ocular delivery in a rat OIR model. Methods: Preretinal neovascularization (NV) was produced in a rat model of oxygen-induced retinopathy (OIR) by modulating inspired oxygen levels between 50% & 10% from P0-P14 in neonatal rat pups, where 50% was maintained for 48 hours from P11-12. From P14-20, 4 litters of rat pups were removed into room air and each litter was randomized into 3 topical QID OU dosing groups, including vehicle (n=18 pups), 0.1% nepafenac (n=23 pups), and 0.5% nepafenac (n=22 pups)At P20, all rats were euthanized and retinas were harvested, ADPase-stained, and prepared as flat mounts. Computerized image analysis was used to determine the median clockhours of preretinal NV per pup in each treatment group. Treatment group medians were compared via nonparametric analyses, where $P<0.05$ was considered significant. Results: Topical ocular delivery of 0.1% nepafenac QID OU significantly inhibited preretinal NV by 55% in this rat OIR model as compared to vehicle ($P=0.02$). Topical ocular delivery of 0.5% nepafenac appeared to decrease preretinal NV >30% however, the difference was not significant. The preretinal NV scores per treatment group were as follows: vehicle = 3.75, 0.1% nepafenac = 1.7, and 0.5% nepafenac = 2.5. Conclusion: Nepafenac, a novel nonsteroidal antiinflammatory prodrug that has rapid corneal penetration, is able to inhibit ischemia-related preretinal NV following topical ocular dosing. The level of antiangiogenic activity provided by topical nepafen is equivalent to a variety of agents tested in rodent OIR models through intravitreal and systemic routes of administration.

IW - ** Major Concepts **
Cardiovascular System (Transport and Circulation)Pharmacology;Sense Organs (Sensory Reception)

- - ** Diseases **
oxygen-induced retinopathy;preretinal neovascularization

- - ** Parts, Structures, Systems of Organisms **
retina: sensory system

- - ** Organisms **
rat (Muridae): neonate

- - ** Taxanotes **
Animals;Chordates; Mammals;Nonhuman Mammals;Nonhuman Vertebrates; Rodents; Vertebrates

- - ** Super Taxa **
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

- - ** Chemicals and Biochemicals **
nepafenac: topical ocular delivery;oxygen

AW - ** Methods and Equipment **

computerized image analysis imaging and microscopy techniques, laboratory techniques

- ** Miscellaneous Descriptors **
  Meeting Abstract

PBC - 86375

PCC - 00520*12512-14504-20004-22002-

PUB - ARVO Annual Meeting Abstract Search and Program Planner
- 2002

CONF - Annual Meeting of the Association For Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA;May 05-10, 2002

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DT - Meeting